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8EHQ-0992-13135

(1)

FORM LG-4878

DUPONT
ESTABLISHED 1802

E. I. DU PONT DE NEMOURS & COMPANY
INCORPORATED
WILMINGTON, DELAWARE 19898

LEGAL DEPARTMENT

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Document Processing Center (TS-790)
Office of Pollution Prevention and Toxics
Environmental Protection Agency
401 M Street., S.W.
Washington, D.C. 20460
Attn: Section 8(e) Coordinator (CAP Agreement)

Dear Coordinator:

8ECAP-0025

On behalf of the Regulatee and pursuant to Unit II B.1.b. and Unit II C of the 6/28/91CAP Agreement, E.I. Du Pont de Nemours and Co. hereby submits (*in triplicate*) the attached studies. Submission of this information is voluntary and is occasioned by unilateral changes in EPA's standard as to what EPA now considers as reportable information. Regulatee's submission of information is made solely in response to the new EPA §8(e) reporting standards and is not an admission: (1) of TSCA violation or liability; (2) that Regulatee's activities with the study compounds reasonably support a conclusion of substantial health or environmental risk or (3) that the studies themselves reasonably support a conclusion of substantial health or environmental risk.

The "Reporting Guide" creates new TSCA 8(e) reporting criteria which were not previously announced by EPA in its 1978 Statement of Interpretation and Enforcement Policy, 43 Fed Reg 11110 (March 16, 1978). The "Reporting Guide states criteria which expands upon and conflicts with the 1978 Statement of Interpretation. Absent amendment of the Statement of Interpretation, the informal issuance of the "Reporting Guide" raises significant due processes issues and clouds the appropriate reporting standard by which regulated persons can assure TSCA Section 8(e) compliance.

For Regulatee,

8ECAP

Mark H. Christman
Counsel
Legal D-7158
1007 Market Street
Wilmington, DE 19898
(302) 774-6443

RECEIVED
6/28/95

ATTACHMENT 1

Submission of information is made under the 6/28/91 CAP Agreement, Unit II. This submission is made voluntarily and is occasioned by recent changes in EPA's TSCA §8(e) reporting standard; such changes made, for the first time in 1991 and 1992 without prior notice and in violation of Regulatee's constitutional due process rights. Regulatee's submission of information under this changed standard is not a waiver of its due process rights; an admission of TSCA violation or liability, or an admission that Regulatee's activities with the study compounds reasonably support a conclusion of substantial risk to health or to the environment. Regulatee has historically relied in good faith upon the 1978 Statement of Interpretation and Enforcement Policy criteria for determining whether study information is reportable under TSCA §8(e), 43 Fed Reg 11110 (March 16, 1978). EPA has not, to date, amended this Statement of Interpretation.

After CAP registration, EPA provided the Regulatee the June 1, 1991 "TSCA Section 8(e) Reporting Guide". This "Guide" has been further amended by EPA, EPA letter, April 10, 1992. EPA has not indicated that the "Reporting Guide" or the April 1992 amendment supersedes the 1978 Statement of Interpretation. The "Reporting Guide" and April 1992 amendment substantively lowers the Statement of Interpretation 's TSCA §8(e) reporting standard[2]. This is particularly troublesome as the "Reporting Guide" states criteria, applied retroactively, which expands upon and conflicts with the Statement of Interpretation.[3] Absent amendment of the Statement of Interpretation, the informal issuance of the "Reporting Guide" and the April 1992 amendment clouds the appropriate standard by which regulated persons must assess information for purposes of TSCA §8(e).

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[2]In sharp contrast to the Agency's 1977 and 1978 actions to soliciting public comment on the proposed and final §8(e) Policy, EPA has unilaterally pronounced §8(e) substantive reporting criteria in the 1991 Section 8(e) Guide without public notice and comment, See 42 Fed Reg 45362 (9/9/77), "Notification of Substantial Risk under Section 8(e): Proposed Guidance".

[3]A comparison of the 1978 Statement of Interpretation and the 1992 "Reporting Guide" is a appended.

Throughout the CAP, EPA has mischaracterized the 1991 guidance as reflecting "longstanding" EPA policy concerning the standards by which toxicity information should be reviewed for purposes of §8(e) compliance. Regulatee recognizes that experience with the 1978 Statement of Interpretation may cause a review of its criteri. Regulatee supports and has no objection to the Agency's amending reporting criteria *provided that* such amendment is not applied to the regulated community in an unfair way. However, with the unilateral announcement of the CAP under the auspices of an OCM enforcement proceeding, EPA has wrought a terrific unfairness since much of the criteria EPA has espoused in the June 1991 Reporting Guide and in the Agency's April 2, 1992 amendment is new criteria which does not.exist in the 1978 Statement of Interpretation and Enforcement Policy.

The following examples of new criteria contained in the "Reporting Guide" that is not contained in the Statement of Interpretation follow:

- o even though EPA expressly disclaims each "status report" as being preliminary evaluations that should not be regarded as final EPA policy or intent[4], the "Reporting Guide" gives the "status reports" great weight as "sound and adequate basis" from which to determine mandatory reporting obligations. ("Guide" at page 20).
- o the "Reporting Guide" contains a matrix that establishes new numerical reporting "cutoff" concentrations for acute lethality information ("Guide" at p. 31). Neither this matrix nor the cutoff values therein are contained in the Statement of Interpretation. The regulated community was not made aware of these cutoff values prior to issuance of the "Reporting Guide" in June, 1991.
- othe "Reporting Guide" states new specific definitional criteria with which the Agency, for the first time, defines as 'distinguishable neurotoxicological effects'; such criteria/guidance not expressed in the 1978 Statement of Interpretation.[5];

- othe "Reporting Guide" provides new review/ reporting criteria for irritation and sensitization studies; such criteria not previously found in the 1978 Statement of Interpretation/Enforcement Policy.
- othe "Reporting Guide" publicizes certain EPA Q/A criteria issued to the Monsanto Co. in 1989 which are not in the Statement of Interpretation; have never been published in the Federal Register or distributed by the EPA to the Regulatee. Such Q/A establishes new reporting criteria not previously found in the 1978 Statement of Interpretation/Enforcement Policy .

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[4]The 'status reports' address the significance, if any, of particular information reported to the Agency, rather than stating EPA's interpretation of §8(e) reporting criteria. In the infrequent instances in which the status reports contain discussion of reportability, the analysis is invariably quite limited, without substantial supporting scientific or legal rationale.

[5] *See, e.g,* 10/2/91 letter from Du Pont to EPA regarding the definition of 'serious and prolonged effects' as this term may relate to transient anesthetic effects observed at lethal levels; 10/1/91 letter from the American Petroleum Institute to EPA regarding clarification of the Reporting Guide criteria.

In discharging its responsibilities, an administrative agency must give the regulated community fair and adequate warning to as what constitutes noncompliance for which penalties may be assessed.

> Among the myriad applications of the due process clause is the fundamental principle that statutes and regulations which purport to govern conduct must give an adequate warning of what they command or forbid.... Even a regulation which governs purely economic or commercial activities, if its violation can engender penalties, must be so framed as to provide a constitutionally adequate warning to those whose activities are governed.

Diebold, Inc. v. Marshall, 585 F.2d 1327, 1335-36 (D.C. Cir. 1978). *See also*, Rollins Environemntal Services (NJ) Inc. v. U.S. Environmental Protection Agency, 937 F. 2d 649 (D.C. Cir. 1991).

While neither the are rules, This principle has been applied to hold that agency 'clarification', such as the Statement of Interpretation, the "Reporting Guide" nor the April 1992 amendments will not applied retroactively.

> ...a federal court will not retroactively apply an unforeseeable interpretation of an administrative regulation to the detriment of a regulated party on the theory that the post hoc interpretation asserted by the Agency is generally consistent with the policies underlying the Agency's regulatory program, when the semantic meaning of the regulations, as previously drafted and construed by the appropriate agency, does not support the interpretation which that agency urges upon the court.

Standard Oil Co. v. Federal Energy Administration, 453 F. Supp. 203, 240 (N.D. Ohio 1978), aff'd sub nom. Standard Oil Co. v. Department of Energy, 596 F.2d 1029 (Em. App. 1978):

The 1978 Statement of Interpretation does not provide adequate notice of, and indeed conflicts with, the Agency's current position at §8(e) requires reporting of all 'positive' toxicological findings without regard to an assessment of their relevance to human health. In accordance with the statute, EPA's 1978 Statement of Interpretation requires the regulated community to use scientific judgment to evaluate the significance of toxicological findings and to determining whether they reasonably support a conclusion of a substantial risk. Part V of the Statement of Interpretation urges persons to consider "the fact or probability" of an effect's occurrence. Similarly, the 1978 Statement of Interpretation stresses that an animal study is reportable only when "it contains reliable evidence ascribing the effect to the chemical." 43 Fed Reg. at 11112. Moreover, EPA's Statement of Interpretation defines the substantiality of risk as a function of both the seriousness of the effect and the probability of its occurrence. 43 Fed Reg 11110 (1978). Earlier Agency interpretation also emphasized the "substantial" nature of a §8(e) determination. See 42 Fed Reg 45362, 45363

(1977). [Section 8(e) findings require "extraordinary exposure to a chemical substance...which critically imperil human health or the environment"].

The recently issued "Reporting Guide" and April 1992 Amendment guidance requires reporting beyond and inconsistent with that required by the Statement of Interpretation. Given the statute and the Statement of Interpretation's explicit focus on substantial human or environmental risk, whether a substance poses a "substantial risk" of injury requires the application of scientific judgment to the available data on a case-by-case basis.

If an overall weight-of-evidence analysis indicates that this classification is unwarranted, reporting should be unnecessary under §8(e) because the available data will not "reasonably support the conclusion" that the chemical presents a substantial risk of serious adverse consequences to human health.

Neither the legislative history of §8(e) nor the plain meaning of the statute support EPA's recent lowering of the reporting threshold that TSCA §8(e) was intended to be a sweeping information gathering mechanism. In introducing the new version of the toxic substances legislation, Representative Eckhart included for the record discussion of the specific changes from the version of H. R. 10318 reported by the Consumer Protection and Finance Subcommittee in December 1975. One of these changes was to modify the standard for reporting under §8(e). The standard in the House version was changed from "causes or contributes to an unreasonable risk" to "causes or significantly contributes to a substantial risk". This particular change was one of several made in TSCA §8 to avoid placing an undue burden on the regulated community. The final changes to focus the scope of Section 8(e) were made in the version reported by the Conference Committee.

The word "substantial" means "considerable in importance, value, degree, amount or extent". Therefore, as generally understood, a "substantial risk" is one which will affect a considerable number of people or portion of the environment, will cause serious injury and is based on reasonably sound scientific analysis or data. Support for the interpretation can be found in a similar provision in the Consumer Product Safety Act. Section 15 of the CPSA defines a "substantial product hazard" to be:

> "a product defect which because of the pattern of defect, the number of defective products distributed in commerce, the severity of the risk, or otherwise, creates a substantial risk of injury to the public."

Similarly, EPA has interpreted the word 'substantial' as a quantitative measurement. Thus, a 'substantial risk' is a risk that can be quantified, *See,* 56 Fed Reg 32292, 32297 (7/15/91). Finally, since information pertinent to the exposure of humans or the environment to chemical substances or mixtures may be obtained by EPA through Sections 8(a) and 8(d) regardless of the degree of potential risk, §8(e) has specialized function. Consequently, information subject to §8(e) reporting should be of a type which would lead a reasonable man to conclude that some type action was required immediately to prevent injury to health or the environment.

Attachment

Comparison:

Reporting triggers found in the 1978 "Statement of Interpretation/ Enforcement Policy",43 Fed Reg 11110 (3/16/78) and the June 1991 *Section 8(e) Guide.*

TEST TYPE	1978 POLICY CRITERIA EXIST?	New 1991 GUIDE CRITERIA EXIST?
ACUTE LETHALITY		
Oral	N}	Y}
Dermal	N}	Y}
Inhalation (Vapors)	}[6]	}[7]
aerosol	N}	Y}
dusts/ particles	N}	Y}
SKIN IRRITATION	N	Y[8]
SKIN SENSITIZATION (ANIMALS)	N	Y[9]
EYE IRRITATION	N	Y[10]
SUBCHRONIC (ORAL/DERMAL/INHALATION)	N	Y[11]
REPRODUCTION STUDY	N	Y[12]
DEVELOPMENTAL TOX	Y[13]	Y[14]

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[6] 43 Fed Reg at 11114, comment 14:

"This policy statements directs the reporitng of specifiec effects when unknown to the Administrator. Many routine tests are based on a knowledge of toxicity associated with a chemicalL unknown effects occurring during such a range test may have to be reported if they are those of concern tot he Agency and if the information meets the criteria set forth in Parts V and VII."

[7] Guide at pp.22, 29-31.

[8] Guide at pp-34-36.

[9] Guide at pp-34-36.

[10] Guide at pp-34-36.

[11] Guide at pp-22; 36-37.

[12] Guide at pp-22

[13] 43 Fed Reg at 11112

"Birth Defects" listed.

[14] Guide at pp-22

NEUROTOXICITY	N	Y[15]
CARCINOGENICITY	Y[16]	Y[17]
MUTAGENICITY		
In Vitro	Y}[18]	Y} [19]
In Vivo	Y}	Y}
ENVIRONMENTAL		
Bioaccumulation	Y}	N
Bioconcentration	Y}[20]	N
Oct/water Part. Coeff.	Y}	N
Acute Fish	N	N
Acute Daphnia	N	N
Subchronic Fish	N	N
Subchronic Daphnia	N	N
Chronic Fish	N	N
AVIAN		
Acute	N	N
Reproductive	N	N
Reprodcutive	N	N

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[15] Guide at pp-23; 33-34.

[16] 43 Fed Reg at 11112
"Cancer" listed

[17] Guide at pp-21.

[18] 43 Fed Reg at 11112; 11115 at Comment 15
"Mutagenicity" listed/ *in vivo* vs *invitro* discussed; discussion of "Ames test".

[19] Guide at pp-23.

[20] 43 Fed Reg at 11112; 11115 at Comment 16.

(9)

CAS # 2783017-7
Chem: 1,12-Dodecanediamine
Title: Approximate Lethal Dose (ALD) of 1,12-Dodecanediamine in Rats
Date: February 29, 1988
Summary of Effects: ALD = 450 mg/kg

Study Title

Approximate Lethal Dose (ALD) of 1,12-Dodecanediamine in Rats

Author

John W. Sarver

Study Completed On

February 29, 1988

Performing Laboratory

E. I. du Pont de Nemours and Company, Inc.
Haskell Laboratory for Toxicology and Industrial Medicine
Elkton Road, P. O. Box 50
Newark, Delaware 19714

Medical Research No.

8272-001

Laboratory Project ID

Haskell Laboratory Report No. 700-87

GENERAL INFORMATION

Material Tested:	1,12-Dodecanediamine
Medical Research No.:	8272-001
Haskell No.:	17,007
Physical Form:	White solid
Purity:	Greater than 99%
Contaminants:	C10 and/or C11 diamines and C12 isomers
Synonyms:	• Dodecamethylenediamine • 1,12-Diaminododecane
Other Codes:	L. Muir 870921-D
CAS Registry No.:	2783-17-7
Stability:	The test material was assumed to be stable under the conditions of administration.
Sponsor:	Du Pont of Canada E. I. du Pont de Nemours and Company, Inc. Kingston, Ontario
Material Submitted By:	Peter Kasserra Du Pont of Canada E. I. du Pont de Nemours and Company, Inc. Kingston, Ontario
In-Life Phase Initiated - Completed:	11/9/87 - 1/29/88
Notebook:	E-51336, pp. 105-116, 141, 152 & 153.

There are 7 pages in this report.

Distribution:	J. Klassen (1) J. H. C. Soule (1) P. Kasserra (1) N. C. Chromey/W. J. Brock (1) J. W. Sarver/A. M. Grandizio (1)

Approximate Lethal Dose (ALD) of 1,12-Dodecanediamine in Rats

SUMMARY

1,12-Dodecanediamine (greater than 99% pure) was administered as a single oral dose by intragastric intubation to male rats. Deaths occurred up to 7 days after dosing. Clinical signs of toxicity were observed in lethally and nonlethally dosed animals. Under the conditions of this test, the ALD was 450 mg/kg of body weight. This material is considered to be moderately toxic (ALD 50 - 500 mg/kg) when administered as a single oral dose.

Work by: Anne M. Grandizio 2125188
Anne M. Grandizio
Technician

Study Director: John W. Sarver 2 125188
John W. Sarver
Technologist

Approved by: William J Brock 2 129188
William J. Brock, Ph.D.
Research Toxicologist
Acute and Developmental Toxicology Section

JWS:alr:HLR700-87(18.3)

QUALITY ASSURANCE DOCUMENTATION

STUDY: MR 8272-001 Approximate Lethal Dose (ALD) of
H# 17,007 1,12-Dodecanediamine in Rats

Because short-term studies are numerous and routine in nature, representative studies from this test type are audited quarterly to ensure the studies are designed and conducted in compliance with the Good Laboratory Practice Standards.

Reported by: Kathleen L Reed 2-16-88
Kathleen L. Reed Date
Quality Assurance Auditor

INTRODUCTION

The purpose of this test was to determine an approximate lethal dose of 1,12-dodecanediamine when administered as a single oral dose to male rats. The ALD was defined as the lowest dose administered which caused death either on the day of dosing or within 14 days post exposure. This study was conducted according to the applicable EPA Good Laboratory Practice Regulations. Areas of noncompliance are documented in the study records. No deviations existed that significantly affected the validity of the study.

MATERIALS AND METHODS

A. Animal Husbandry

Male Crl:CD®BR rats, approximately 7 weeks old, were received from Charles River Breeding Laboratories, Kingston, New York. Rats were housed singly in suspended, stainless steel, wire-mesh cages. Each rat was assigned a unique identification number which was recorded on a card affixed to the cage. Purina Certified Rodent Chow® #5002 and water were available ad libitum. Rats were quarantined, weighed, and observed for general health for approximately one week prior to testing. Animal rooms were maintained on a timer-controlled, 12-hour light/12-hour dark cycle. Environmental conditions of the rooms were targeted for a temperature of 23 ± 2°C and relative humidity of 50 ± 10%. Excursions outside these ranges were of small magnitude and/or brief duration and did not adversely affect the validity of the study.

B. Protocol

The test material was suspended in Mazola® corn oil and administered to one rat per dose rate by intragastric intubation. Dose rates administered ranged from 200 to 5000 mg/kg of body weight in increments of approximately 50%. The dosing day was test day one; postexposure day 14 was test day 15. Following administration of the test material, rats were observed for clinical signs of toxicity. Surviving rats were weighed and observed daily until signs of toxicity subsided, and then at least 3 times per week throughout the 14-day postexposure period. Observations for mortality were made daily throughout the study.

C. Records Retention

All raw data and the final report will be stored in the archives of Haskell Laboratory for Toxicology and Industrial Medicine, E. I. du Pont de Nemours and Company, Inc., Newark, Delaware or in the Du Pont Records Management Center, Wilmington, Delaware.

RESULTS

The dosage regimen and the mortality resulting over the 15-day test period are detailed below.

First Study

Dosage (mg/kg)	Dose Volume (mL)	Suspension Concentration (mg/mL)	Initial Body Weight (g)	Mortality
300	0.8	100	268	No
450	1.2	100	260	Yes
670	0.56	300	250	No
1000	1.3	200	254	No
1500	1.8	200	245	Yes
2300	2.0	300	255	Yes
3400	2.9	300	253	Yes
5000	4.3	300	259	Yes

In the first study, the lowest dose of 1,12-dodecanediamine that resulted in the death of a test animal was 450 mg/kg. Rats dosed at 300, 670 or 1000 mg/kg survived. The rats dosed at 300 or 1000 mg/kg exhibited numerous clinical signs of toxicity and slight to severe weight losses (up to 28% of initial body weight). No weight loss or clinical signs of toxicity were observed in the rat dosed at 670 mg/kg. Because of the similarity in clinical signs of toxicity observed between the rats dosed at 300, 450 or 1000 mg/kg and the variability in mortality, a second study was conducted to more accurately define the ALD.

Second Study

Dosage (mg/kg)	Dose Volume (mL)	Suspension Concentration (mg/mL)	Initial Body Weight (g)	Mortality
200	1.1	50	266	No
300	1.6	50	260	No
450	1.2	100	265	No
670	1.8	100	262	Yes
1000	2.7	100	273	Yes
1500	3.9	100	259	Yes

Clinical Signs

In the first study, the rats dosed at 300, 450 or 1000 mg/kg exhibited lethargic behavior, lung noise and wet or stained perineum. Additionally, the rats dosed at 450 or 1000 mg/kg exhibited stained fur and ocular, nasal or oral discharges. The rat dosed at 450 mg/kg was bloated from test day 4 until found dead 7 days after dosing. These rats had slight to severe weight losses (up to 38% of initial body weight) up to 6 days after dosing. Rats dosed at 1500 mg/kg and higher were found dead one day after dosing.

In the second study, the clinical signs of toxicity exhibited by the rats were similar to the clinical signs exhibited by rats from the first study. The rats dosed at 300, 670 or 1000 mg/kg exhibited lethargic behavior; wet or stained perineum; ocular, nasal or oral discharges and lung noise or labored breathing. The rat dosed at 1000 mg/kg also exhibited gasping and hunched posture. These rats had severe weight losses (up to 24% of initial body weight) up to 2 days after dosing. The rat dosed at 1500 mg/kg died before clinical signs of toxicity were apparent. Deaths occurred up to 3 days after dosing. The rat dosed at 450 mg/kg had a slight body weight loss one day after dosing but exhibited no clinical signs of toxicity throughout the study.

CONCLUSION

Under the conditions of this study, the ALD for 1,12-dodecanediamine was 450 mg/kg of body weight. This material is considered to be moderately toxic (ALD 50 - 500 mg/kg) when administered as a single oral dose.

Triage of 8(e) Submissions

Date sent to triage: _____ NON-CAP (CAP)

Submission number: 13135A TSCA Inventory: (Y) N D

Study type (circle appropriate):

Group 1 - Dick Clements (1 copy total)

ECO AQUATO

Group 2 - Ernie Falke (1 copy total)

(ATOX) SBTOX SEN w/NEUR

Group 3 - Elizabeth Margosches (1 copy each)

STOX CTOX EPI RTOX GTOX

STOX/ONCO CTOX/ONCO IMMUNO CYTO NEUR

Other (FATE, EXPO, MET, etc.): _____

Notes:

THIS IS THE ORIGINAL 8(e) SUBMISSION; PLEASE REFILE AFTER TRIAGE DATABASE ENTRY

For Contractor Use Only

entire document: (0) 1 2 **pages** 1,9 **pages** _____

Notes:

Contractor reviewer : JW **Date:** 1/24/96

CECATS\TRIAGE TRACKING DBASE ENTRY FORM

CECATS DATA:
Submission # 8EHQ-0992-13135 SEQ. A

TYPE: (INT) SUPP FLWP

SUBMITTER NAME: E. I. Dupont de Nemours and Company

INFORMATION REQUESTED: FLWP DATE:
0501 NO INFO REQUESTED
0502 INFO REQUESTED (TECH)
0503 INFO REQUESTED (VOL ACTIONS)
0504 INFO REQUESTED (REPORTING RATIONALE)

DISPOSITION:
(0639) REFER TO CHEMICAL SCREENING
(0678) CAP NOTICE

VOLUNTARY ACTIONS:
(0601) NO ACTION REPORTED
0602 STUDIES PLANNED/UNDERWAY
0603 NOTIFICATION OF WORKER PROTECTION
0604 LABEL/MSDS CHANGES
0605 PROCESS/HANDLING CHANGES
0606 APP/USE DISCONTINUED
0607 PRODUCTION DISCONTINUED
0608 CONFIDENTIAL

SUB. DATE: 09/11/92 OTS DATE: 09/22/92 CSRAD DATE: 05/28/95

CHEMICAL NAME:

CAS#
2783-17-7

INFORMATION TYPE:		P F C
0201	ONCO (HUMAN)	01 02 04
0202	ONCO (ANIMAL)	01 02 04
0203	CELL TRANS (IN VITRO)	01 02 04
0204	MUTA (IN VITRO)	01 02 04
0205	MUTA (IN VIVO)	01 02 04
0206	REPRO/TERATO (HUMAN)	01 02 04
0207	REPRO/TERATO (ANIMAL)	01 02 04
0208	NEURO (HUMAN)	01 02 04
0209	NEURO (ANIMAL)	01 02 04
0210	ACUTE TOX. (HUMAN)	01 02 04
0211	CHR. TOX. (HUMAN)	01 02 04
(0212)	ACUTE TOX. (ANIMAL)	01 (02) 04
0213	SUB ACUTE TOX (ANIMAL)	01 02 04
0214	SUB CHRONIC TOX (ANIMAL)	01 02 04
0215	CHRONIC TOX (ANIMAL)	01 02 04

INFORMATION TYPE:		P F C
0216	EPI/CLIN	01 02 04
0217	HUMAN EXPOS (PROD CONTAM)	01 02 04
0218	HUMAN EXPOS (ACCIDENTAL)	01 02 04
0219	HUMAN EXPOS (MONITORING)	01 02 04
0220	ECO/AQUA TOX	01 02 04
0221	ENV. OCCC/REL/FATE	01 02 04
0222	EMER INCI OF ENV CONTAM	01 02 04
0223	RESPONSE REQEST DELAY	01 02 04
0224	PROD/COMP/CHEM ID	01 02 04
0225	REPORTING RATIONALE	01 02 04
0226	CONFIDENTIAL	01 02 04
0227	ALLERG (HUMAN)	01 02 04
0228	ALLERG (ANIMAL)	01 02 04
0239	METAB/PHARMACO (ANIMAL)	01 02 04
0240	METAB/PHARMACO (HUMAN)	01 02 04

INFORMATION TYPE:		P F C
0241	IMMUNO (ANIMAL)	01 02 04
0242	IMMUNO (HUMAN)	01 02 04
(0243)	CHEM/PHYS PROP	01 02 04
0244	CLASTO (IN VITRO)	01 02 04
0245	CLASTO (ANIMAL)	01 02 04
0246	CLASTO (HUMAN)	01 02 04
0247	DNA DAM/REPAIR	01 02 04
0248	PROD/USE/PROC	01 02 04
0251	MSDS	01 02 04
0299	OTHER	01 02 04

TRIAGE DATE:

NON-CBI INVENTORY
(YES)
NO
UNDETERMINED

ONGOING REVIEW
YES (DROP/REFER)
NO (CONTINUE)
REFER

SPECIES
RAT

TOXICOLOGICAL CONCERN:
LOW
MED Acute oral Toxicity
HIGH

USE:

PRODUCTION:

CAS SR

COMMENTS

13135A

M

Acute oral toxicity in the rat is of medium concern based on an approximate lethal dose of 450 mg/kg. In the first study, single oral doses (1/group) of 300, 450, 670, 1000, 1500, 2300, 3400, and 5000 mg/kg were administered to male rats. Deaths occurred in rats dosed at 450 and ≥1500 mg/kg. Clinical signs of toxicity included lethargy, lung noise, wet or stained perineum (300, 450, 1000 mg/kg), ocular, nasal, or oral discharges (450, 1000 mg/kg), and slight to severe weight loss (450 mg/g). A second study was conducted to more accurately define the approximate lethal dose because of the similarity in clinical signs of toxicity observed between rats dosed at 300, 450, or 1000 mg/kg and the variability of mortality in the first study. In the second study, single oral doses (1/group) of 200, 300, 450, 670, 1000, and 1500 mg/kg were administered to male rats. Deaths occurred in rats dosed at ≥670 mg/kg. Clinical signs exhibited in the second study were similar to those in the first.